REMARKS

Claim Amendments

Applicants have amended claims 17 and 20 to be in independent format. Applicants have amended claim 21 to make it depend also from claims 17 and 20.

These amendments add no new matter. Their entry is requested.

Withdrawn Rejections/Objections

Applicants acknowledge with appreciation the Examiner's indication that any outstanding rejection/objection not expressly maintained in the January 5, 2006 Office Action is withdrawn or rendered moot.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 11-25 and 30 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. According to the Examiner, "the specification, while being enabling for a compound of formula (I), does not reasonably provide enablement for the instantly claimed compounds of formula (III) or the tautomers thereof or the pharmaceutically acceptable salts thereof." Office Action, page 2. The Examiner contends that the specification does not enable the skilled artisan to make and/or use the invention commensurate in scope with the claims. In particular, the Examiner contends that the specification fails to enable the preparation of the entire scope of the claimed compounds and fails to enable one skilled in the art to use the claimed compounds. Applicants traverse.

Applicants disagree that the specification does not enable the preparation of the entire scope of the compounds of the pending claims. As noted by the Examiner, the specification discloses the preparation of compounds of Formula I with a bicyclic ring system. One of skill in the art would understand that the scheme shown in Example 1 for the synthesis of compounds of Formula I could be readily adapted to synthesize the compounds of Formula III. For example, the reaction to convert Compound 5 to Compound 6, as shown at specification pages 30-31, could be adapted by the use of 2,6-dichloropyridine—or a "W"-substituted 2,6-dichloropyridine—in place of 3,6 dichloropyridazine. Introduction of a Q_2 moiety into the pyridine ring of the product of this reaction and conversion of the nitrile group to an amide would directly result in compounds of Formula III wherein "Z" is "N". The Q_2 moiety could be introduced, for example, by reaction of the pyridine intermediate with an aryl lithium compound or an aryl metallic compound as is well known in the art. Alternatively, a Q_2–containing chloropyridine could be reacted with Compound 5 to generate the penultimate product directly. Conversion of the nitrile group to an amide could be accomplished, for example, as shown for the conversion of Compound 9 to Compound 10 at specification page 31.

Compounds of Formula III wherein "Z" is "N" could be synthesized in a similar manner, for example by reaction of Q_1–NH_2 with 2,6-dibromopyridine in the presence of a base, reaction of the product of this reaction with a Q_2–boronic acid in the presence of a palladium catalyst, and acylation of the bridging nitrogen to generate a compound of Formula III. The skilled artisan would appreciate that the Q_2–boronic acid could alternatively be reacted with 2,6-dibromopyridine prior to the reaction with Q_1–NH_2.

All of the above starting materials and reactions were well known in the art at the time of the application. See, e.g., PCT International Publication No. WO 98/27098, cited at specification page 3, line 2.

Applicants also disagree that the specification does not enable one of skill in the art to use the compounds of the pending claims. For example, the specification discloses that substituted nitrogen-containing heterocycles may function as p38 inhibitors. See specification page 3. The specification also provides *in vitro* assays useful for determining that the compounds of the present invention are inhibitors of p38 activity, inhibitors of IL-1, TNF, IL-6, and IL-8 production, and inhibitors of LPS-induced prostaglandin endoperoxide synthase-2 induction. See specification page 19 and specification pages 37-42. The specification also provides *in vivo* assays useful for determining the effects of the claimed compounds in animal models of disease. See specification pages 19-20. As described in detail in applicants' March 18, 2005 Amendment and Reply, the specification discloses the relationship between the inhibition of p38, the blockade of production of pro-inflammatory proteins, and the treatment of disease. For the above reasons, applicants maintain that the specification fully enables the skilled artisan to make and use the invention commensurate in scope with the claims. Applicants therefore respectfully request that the objection be withdrawn.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 17 and 20 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the

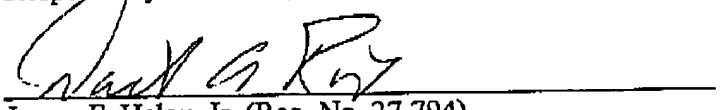
Examiner, there is insufficient antecedent basis for "compound 15" and "compound 18"in the compounds of claim 11.

In response to the rejection, applicants have obviated any possible lack of antecedent basis in claims 17 and 20 by amending these claims to independent format. Applicants respectfully request that the rejections be withdrawn in light of these amendments.

Conclusion

In view of the above, applicants request that the Examiner enter the above amendments, consider the accompanying arguments, withdraw the rejections, and allow the pending claims to pass to issue.

Respectfully submitted,



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